REMARKS

Status of the Claims

Claims 1-15 and 58-68 were pending. Claims 59-67 are canceled without prejudice or disclaimer. Applicants reserve the right to prosecute cancelled subject matter in one or more divisional or continuation applications. Claim 58 is amended. No new matter has been added by the amendment.

Applicants thank the Examiner for withdrawing the rejections made in the previous office action and provide the following remarks regarding the new grounds of rejections raised in the Action.

35 U.S.C. § 112, Second Paragraph, Indefiniteness

Claims 1, 58-60, 63 and 65 were rejected for being indefinite. As an initial matter, Applicants submit that the grounds for rejection for claim 1 have not been set forth in the Action leading the Applicants to believe that inclusion of claim 1 in this rejection here was a typographical error. Furthermore, Claims 59, 60, 63 and 65 have been cancelled. Accordingly, Applicants present arguments related to the indefiniteness rejection of Claim 58 only.

Claim 58

The Action states that "Claim 58, steps i)-iii) are confusing in relation to claim 1 from which claim 58 depends because it is unclear how steps i)-iii) functionally and cooperatively relate to the method steps recited in claim 1. If steps i)-iii) are intended to be performed in a specific order congruous to the method steps in claim 1, steps a) and b), i.e. as an example: a) - i) - ii) - b) - iii); then such should be clearly defined to render the instant claim definite." Further, "Claim 58 step ii) is confusing in relation to step i) because it is unclear what essential functional cooperative relationship exists between the fetal cells in step ii) and the isolated PBMC in step i). Are the fetal cells parts of the isolated fraction in step i)?"

Solely in the interest of advancing prosecution, Applicants have amended claim 58 so that it is in independent form and no longer depends from Claim 1. Support for the amendment can be found throughout the application, at least at paragraphs [0041] to [0044] of the published application.

Further, in response to the Examiner's question regarding the relationship between the fetal cells and the PBMCs, as explained in paragraph [0045] (page 8, lines 17-22 of the application, as filed), the term "PBMCs" or "PBMC fraction" or similar term refers to nucleated cells isolated from maternal blood, such as, for example, following purification of blood on Ficoll and "[a]s will be known to the skilled artisan, a preparation of PBMCs or isolated PBMCs is a fraction of the maternal blood that comprises a mixture of cells, including fetal cells. Accordingly, the fetal cells are isolated with maternal PBMCs in such a nucleated cellular fraction." Thus, as explained in the specification, fetal cells are part of the isolated PBMC fraction. To further clarify this point, Applicants have inserted the term "fetal cells from the fraction" in step (iii).

Applicants respectfully submit that in view of these amendments and remarks, this rejection should be withdrawn.

35 U.S.C. § 112, First Paragraph, Enablement

Claims 1-15 and 58-68 are rejected under 35 U.S.C. 11 2, first paragraph, as failing to comply with the enablement requirement. "The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." MPEP 2164.01, citing *United States v. Telectronics, Inc.*, 857 F.2d 778, 785, (Fed. Cir. 1988). Applicants respectfully submit that the claims of the present invention meet the enablement requirement.

A common theme of the assertions in the enablement rejection is that the specification does not provide secondary antibodies (or other agents) which will "*specifically and exclusively* detect and identify fetal cell-maternal antibody complexes that *specifically* consist of fetal cells carrying paternally inherited fetal antigen." (emphasis added.)

However, nowhere in the specification is it suggested that the secondary antibody have such specificity. Furthermore, it is clear from the specification as filed, particularly the Examples, that such specificity is not required to practice the claimed invention.

The claimed invention is based on the principle that the mother's immune system recognizes paternally-derived antigens (that are not naturally present in the mother) as foreign, and hence, an immune response is generated against these paternally-derived antigens. Despite this immune response, there are mechanisms that generally ensure that this immune response

does not affect the developing fetus (there are exceptions such as those leading to recurrent spontaneous abortion). The present inventors have devised mechanisms of using this natural immune response to paternally-derived antigens to detect and isolate fetal cells. Since there are complex mechanisms which ensure that a body does not mount an immune response to self-antigens, in a pregnant female a significant proportion of circulating antibodies will bind to paternally derived antigens on fetal cells and not to maternal antigens. Following from this, there is no need to have an agent, such as a secondary antibody, that selectively binds antibodies that bind paternally-derived antigens to practice the invention. It is sufficient that the agent bind to maternal antibodies (which are in turn only bound to paternal antigens on the fetal cells).

This is clearly exemplified in Example 1 of the specification, as filed, where *non-selective* secondary antibodies were used (namely, a mixture of goat F(ab')2 antihuman IgG and goat F(ab')2 anti-human IgM) to bind maternal antibodies bound to fetal cells to detect and enrich these fetal cells.

Thus, based on the data reported in Example 1, it is apparent that the assertions with regard to the requirement of a specific secondary antibody or similar molecules are based on a lack of understanding of the workings of the claimed invention. Such an antibody is not required to practice the claimed invention, and one skilled in the art will understand how to practice the claimed invention based on what is disclosed in the specification and what is known in the art. Applicants, therefore, respectfully request that the enablement rejection be withdrawn.

Conclusion

For the reasons stated above, Applicants respectfully submit that all pending claims are now in condition for allowance. For any questions, the Examiner is requested to contact the undersigned at the phone number given below.

Respectfully submitted,
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